REMARKS

Claims 1-10 and 31 remain pending. The Applicants respectfully request reconsideration of the patentability of these claims based on the following remarks.

Obviousness

Claims 1-10 and 31 were rejected under 35 U.S.C. § 103(a) as being unpatentable over Hashmi et al. (WO 01/07079). Hashmi et al. relates to a vaccine formulation that provides for the extended release of antigenic material over time. The Examiner pointed out that the reference contemplates a variation wherein a relatively constant release rate is periodically supplemented with a burst of higher release (page 10, lines 7-10). This embodiment is used to trigger the immune system to remain highly active over time.

However, knowledge of the disclosure of Hashmi et al. would not lead one having ordinary skill in the art to produce the presently claimed invention. The present invention requires that "progressively increasing doses" of biologically active agents be released "over a predetermined period of time." As explained below, nothing in Hashmi et al. would lead one having ordinary skill in the art to such a method.

Hashmi et al. suggests that the shape of the device can be chosen to perfect both initial release rates and the effect of any tailing off thereof (page 12, lines 23-25). In a further variation, the device can have multiple layers or graduated layers allowing for differing release rate profiles. For example, referring to Hashmi et al. at page 12, line 26 through page 13, line 4, Hashmi et al. discloses an embodiment that has the following four components:

1. A core layer allowing for a "relatively high" release rate;
2. A first surrounding layer with a "low" release of active material;
3. A second surrounding layer with a "relatively high" release rate; and
4. A protective coating.

Delivery of active material would occur in reverse order. After the protective coating was dissolved, the second surrounding layer would deliver at a "relatively high" release rate, followed by a "low" release period, followed by a "relatively high" release rate from the core. The Examiner stated that this embodiment suggests progressively increasing doses with one single administration/device. However, contrary to the Examiner's assertion, Hashmi et al. merely indicates that there are two layers that exhibit a "relatively high" release rate in comparison to an intervening layer that exhibits a "low" release of active material. The doses provided by the

second surrounding layer and the core are "relatively high" in comparison to the "low" release layer, but there is nothing in the reference that teaches that the core layer provides a higher dose when compared with the second surrounding layer. Thus, contrary to the Examiner's assertion, Hashmi et al. does not suggest progressively increasing doses with one single administration/device.

The proper analysis for determining obviousness is set forth in MPEP 2141. That section of the MPEP describes how the Supreme Court in *KSR International Co. v. Teleflex Inc. (KSR)*, 550 U.S. ___, 82 USPQ2d 1385 (2007), reiterated the framework for the objective analysis for determining obviousness under 35 U.S.C. § 103(a) as stated in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966). Obviousness is a question of law based on underlying factual inquiries. The factual inquiries enunciated by the Court are as follows:

(A) Determining the scope and content of the prior art;

(B) Ascertaining the differences between the claimed invention and the prior art; and

(C) Resolving the level of ordinary skill in the pertinent art.

In addition, objective evidence relevant to the issue of obviousness must also be evaluated by Office personnel. The following addresses these criteria in relation to the present Office Action.

A. Determining the Scope and Content of the Prior Art

The Examiner is correct insofar as the Hashmi et al. specification does disclose the single administration of a sensitizing and booster dosage of an antigen. However, as was previously submitted, it is well known in the art that a booster dosage is a dose of an active immunization agent, usually smaller than the initial dose, which is given to maintain immunity. Referring to the attached entry for "booster dose" from the Dorlands Medical Dictionary website, a booster dose is defined as:

> an amount of immunogen (vaccine, toxoid, or other antigen preparation), usually smaller than the original amount, injected at an appropriate interval after primary immunization to sustain the immune response to that immunogen.

The Dorlands Medical Dictionary also defines "dose" as:

> the quantity to be administered at one time, as a specified amount of medication or a given quantity of radiation.

Furthermore, as can be seen from the passages relied on by the Examiner above, Hashmi et al. is solely concerned about the ability to alter the release rates between the sensitizing and booster

dosages. Indeed, Hashmi et al. is completely silent as to increasing the amounts of the subsequent dosages.

2. Ascertaining the Differences Between the Claimed Invention and the Prior Art

A key difference between what is taught in Hashmi et al. in comparison to the claims of the present invention is that Hashmi et al. does not teach or suggest a single administration of two or more progressively increasing dosages of an antigen. By way of contrast Hashmi et al. is solely concerned with manipulating the release rates of a sensitizing and booster dosage. As was mentioned above, a booster dosage is smaller than that of the initial sensitizing dosage. Hashmi et al. merely indicates that a booster dose can be released at a faster rate, without indicating anything about the size of the booster dose. Thus, the disclosure of Hashmi lacks any teaching of the presently claimed "progressively increasing doses."

Of course, the skilled artisan would also have knowledge of the conventional protocol for delivering vaccines. The features of the conventional protocol are discussed in the Specification as filed at page 13, lines 2-8, and Figure 1 shows the development of an anamnestic response. Thus, the skilled artisan would be aware that the conventional protocol for delivering vaccines is via two injections, administered approximately one month apart. Ideally, the antibody response to the first injection will have begun to wane before the second injection. The second injection is more successful in stimulating clonal expansion of antibody-forming cells, which were developed in response to the first injection. A third injection may be given three to twelve months later and causes the so called anamnestic response, wherein increased clonal expansion occurs and long-lived antibody-forming cells are stimulated.

Thus, neither Hashmi et al. nor the general knowledge of those having ordinary skill in the art provide any teaching of the recited "progressively increasing doses." Nor would anything in Hashmi et al. or the general knowledge of those having ordinary skill provide any reason to develop a method having such a feature.

3. Resolving the Level of Ordinary Skill in the Pertinent Art

Although the level of skill in the art is relatively high, requiring substantial education, a person having ordinary skill in the art would not have any basis to produce the presently claimed invention based only knowledge of Hashmi and the conventional knowledge of those having ordinary skill in the art. As discussed above, neither Hashmi et al. nor the conventional

knowledge provide any reason to produce a method that delivers the recited "progressively increasing doses." Accordingly, no proper *prima facie* showing of obviousness can be established on the basis of the Hashmi et al. reference.

4. Considering Objective Evidence Present in the Application indicating Obviousness or Non-Obviousness

As discussed above, a distinguishing feature of the presently claimed vaccination regimen is that progressively increasing dosages mimic the growth of bacteria during an episode of infection and the natural antibody response thereto. Referring to page 5 line 25 and page 6 lines 1 to 4 of the specification, the progressively increasing doses of antigen are chosen to elicit an optimal antibody response, which includes the production of both high-affinity antibodies and antigen-specific memory lymph sites. Objective evidence as to the benefits of administering progressively increasing doses (which is absent in Hashmi et al.) can be found in the Specification as filed on page 17, line 16 - page 18, line 14 and Figure 5, where progressively increasing doses were shown to be more effective in stimulating an early antibody response compared to a conventional vaccination regimen. Moreover, referring to the Specification as filed at page 14, lines 11 to 13, there is no record of research that attempts to duplicate a proliferative disease, which tends to provide antigen exponentially to the host until the host has fully responded and destroyed and pathogen. Thus, not only would one of skill in the art not have had any reason to develop the presently claimed processes based on the prior art or record, but such a skilled person would find the results achieved by the present invention completely unexpected. These unexpected results are further evidence of the nonobviousness of the presently claimed invention.

In view of the preceding remarks, the claimed invention and results achieved by the present invention are neither discussed nor contemplated by Hashmi et al. Accordingly, the present claims are not obvious and the Applicants respectfully request that the rejection be withdrawn.

No Disclaimers or Disavowals

Although the present communication may include alterations to the application or claims, or characterizations of claim scope or referenced art, Applicant is not conceding in this application that previously pending claims are not patentable over the cited references. Rather,

any alterations or characterizations are being made to facilitate expeditious prosecution of this application. Applicant reserves the right to pursue at a later date any previously pending or other broader or narrower claims that capture any subject matter supported by the present disclosure, including subject matter found to be specifically disclaimed herein or by any prior prosecution. Accordingly, reviewers of this or any parent, child or related prosecution history shall not reasonably infer that Applicant has made any disclaimers or disavowals of any subject matter supported by the present application.

CONCLUSION

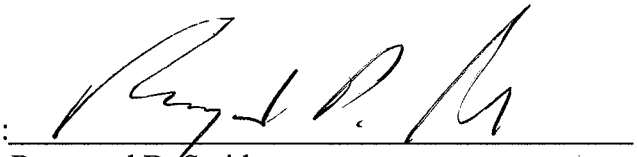
In view of the foregoing Remarks, it is respectfully submitted that the present application is in condition for allowance. Should the Examiner have any remaining concerns which might prevent the prompt allowance of the application, the Examiner is respectfully invited to contact the undersigned at the telephone number appearing below.

Please charge any additional fees, including any fees for additional extension of time, or credit overpayment to Deposit Account No. 11-1410.

Respectfully submitted,

KNOBBE, MARTENS, OLSON & BEAR, LLP

Dated: August 20, 2009

By: 

Raymond D. Smith
Registration No. 55,634
Agent of Record
Customer No. 20995
(949) 760-0404

7638079
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